



COVID-19 and its impact on the brain and Mind- A conceptual model and supporting evidence

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel coronavirus that is causing the ongoing coronavirus disease 2019 (COVID-19) pandemic, was first reported in late 2019. Since then, an unprecedented amount of new knowledge has emerged about this virus and its treatment. Although the reported symptoms of COVID-19 are primarily respiratory with acute respiratory distress syndrome, SARS-CoV-2 has also been shown to affect other organs, including brain, and there are growing reports of neuropsychiatric symptoms due to COVID-19. There are two suggested pathways for how COVID-19 can affect the brain and mind: the direct impact on the brain and impact mediated via stress. Direct impact on the brain is manifested as encephalitis/encephalopathy with altered mental status (AMS) and delirium. In this paper, we summarize evidence from studies of previous outbreaks and current data from the COVID-19 pandemic that describe how COVID-19 is associated with an increased prevalence of anxiety, stress, poor sleep quality, obsessive-compulsive symptoms, and depression among the general population during the pandemic. In addition, we summarize the current evidence that supports how COVID-19 can also impact the CNS directly and result in delirium, cerebrovascular events, encephalitis, unspecified encephalopathy, AMS, or peripheral neurologic disorders.

Keywords COVID-19 · SARS-CoV-2 · Stress response · Psychiatric disorder · Mental health · Neuropsychiatric disorders · Cerebrovascular events

Introduction

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the novel coronavirus that is causing the ongoing coronavirus disease 2019 (COVID-19) pandemic, was first reported in late 2019 [1]. As of early October 27, 2021, more than 244 million confirmed

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cases of COVID-19 had been reported worldwide, and the United States has been the most affected country with over 45 million confirmed cases [2]. Although the reported symptoms of COVID-19 are primarily respiratory with acute respiratory distress syndrome, SARS-CoV-2 has also been shown to affect other organs, including the brain, and there are emerging reports of neuropsychiatric symptoms due to COVID-19 [3], [4]. Physical and social isolation, the disruption of daily routines, financial stress, food insecurity, and numerous other potential triggers for stress response have all been intensified due to this pandemic, creating a situation in which many individuals' mental well-being and stability are threatened. The uncertain environment is likely to increase the frequency and/or severity of mental health problems worldwide. Psychiatric symptoms such as anxiety and depression have been reported among patients with SARS-CoV-1 during the previous severe acute respiratory syndrome (SARS) epidemic [5], [6]. Alcohol use, post-traumatic stress disorder (PTSD), anxiety, anger, fear of contagion, uncertainty, and distrust are a few of the immediate, and likely long-term effects, from the COVID-19 pandemic. In this paper, we summarize evidence from studies of previous outbreaks and early data from the COVID-19 pandemic that suggests that during outbreaks, health care workers experience high levels of psychological symptoms. We'll describe how COVID-19 is also associated with an increased prevalence of anxiety, stress, poor sleep quality, obsessive-compulsive symptoms, and depression among the general population during the pandemic. We will summarize the current evidence that supports how COVID-19 can impact the CNS directly and result in delirium, cerebrovascular events, encephalitis, unspecified encephalopathy, altered mental status (AMS), or peripheral neurologic disorders. Patients with preexisting psychiatric disorders are also likely to have increased symptoms and should be monitored for breakthrough symptoms and acute exacerbations. [1]–[6].

An unprecedented amount of new knowledge has emerged about this virus and its treatment. The table below summarizes the major achievement in our understanding of the COVID-19:

A COVID-19 Timeline

January 9, 2020	WHO Announces Mysterious Coronavirus-Related Pneumonia in Wuhan, China
January 10	The first SARS-COV-2 genome sequence is released online (Holmes EC, Novel YZ. 2019 coronavirus genome, 2020)
January 21	CDC Confirms First US Coronavirus Case in Washington State
March 11	WHO Declares COVID-19 a Pandemic
March 17	The University of Minnesota Begins Testing Hydroxychloroquine
April 29	NIH Trial Shows Early Promise for Remdesivir
June 20	NIH Halts Trial of Hydroxychloroquine
July 29	FDA Grants Truvian EUA for Rapid Antibody Test
August 23	Convalescent Plasma is Cleared for Use by FDA
September 3	Steroids Reduce Mortality in Severe Cases
October 22	FDA Approves Remdesivir as First COVID-19 Drug
December 11	FDA Agree to EUA for COVID-19 Vaccine from Pfizer, BioNTech
December 18	FDA Agree to EUA for COVID-19 Vaccine from Moderna's
February 27, 2021	FDA Agree to EUA for COVID-19 single-dose Vaccine from Johnson & Johnson
May 10	FDA Authorizes Pfizer-BioNTech COVID-19 Vaccine for Emergency Use in Adolescents
August 12	FDA Authorizes Additional Vaccine Dose for Immunocompromised People
October 29	FDA Authorizes COVID-19 Vaccine in Children 5–11

Pandemics have a global reach of mass destruction and historically have been more devastating than any other type of disaster. In the past decade before COVID-19, outbreaks of SARS, H1N1 “swine flu”, MERS, Ebola, and Zika resulted in significant morbidity and mortality and highlighted the mental health issues associated with a pandemic outbreak [6], [7]. The pandemics can threaten our psychological well-being through:

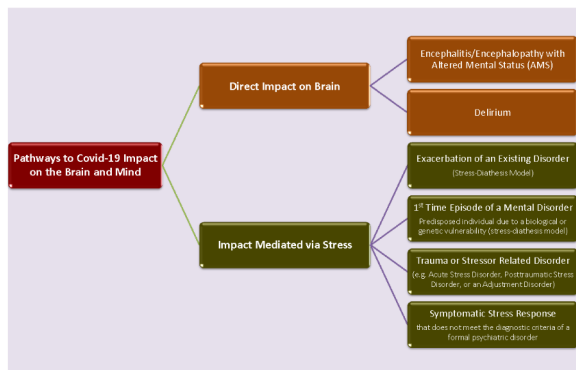
- Stress related to isolation and loneliness; unemployment; food and shelter insecurity; and socioeconomic stress.
- Parental stress about children.
- Stress-related illnesses in patients, families and caregivers (burnout and moral injury, compassion fatigue and secondary PTSD).
- Psychotic decompensations in patients with serious mental illness (SMI).
- Symptoms of grief, depression, anxiety, PTSD and insomnia.
- Suicide risk: separation and loss, unemployment, family strife, civic unrest.

Understanding how the pandemic can affect our psychological well-being requires an understanding of how the causative agent, SARS-CoV-2, can affect our brain and mind. There are two suggested pathways for how COVID-19 can affect the brain and mind: the direct impact on the brain and impact mediated via stress. Direct impact on the brain is manifested as encephalitis/encephalopathy with AMS and delirium.

Impact mediated via stress includes a stress diathesis model where a disorder develops from an individual’s genetic predisposition for developing that illness combined with stressful conditions that play a precipitating or facilitating role. Stress can also cause exacerbation of an existing psychiatric disorder, trauma or stress-related disorders, or symptomatic stress response which does not meet diagnostic criteria for formal psychiatric diagnosis.

The figure 1 below provides a conceptual model regarding how SARS-CoV-2 can impact the brain and the mind:

Fig. 1 Pathways to COVID-19 Impact on Brain and Mind



Central Nervous System (CNS) Involvement:

The first case of viral encephalitis associated with SARS-CoV-2 was reported on March 4, 2020, at Beijing Ditan Hospital. The researchers confirmed the presence of SARS-CoV-2 in the cerebrospinal fluid (CSF) by genome sequencing [8]. Subsequently, another case of SARS-CoV-2 encephalitis was reported in Japan where SARS-CoV-2 was identified in the CSF in the absence of nasopharyngeal positivity. This raised the possibility of direct infection or alternate routes of transmission such as hematogenous [9]. Since then, there have been numerous cases of neurological involvement associated with SARS-CoV-2. Studies have shown that the genetic material and protein of viruses can be detected in CNS samples indicating direct CNS invasion and neuronal tissue damage [10], [11].

SARS-CoV-2, like SARS and MERS, can cause delirium, agitation, and altered consciousness, as well as symptoms of depression, anxiety, and insomnia.

Other manifestations of CNS involvement may include:

- Loss of smell and loss of taste.
- Headache.
- Stroke.
- Seizure.
- Motivation and Movement changes.

Hierarchical clustering analysis showed that neuropsychiatric symptoms group together in three distinct groups [12]:

1. anosmia (loss of smell) and hypogeusia (loss of taste).
2. dizziness and headache.
3. photophobia, mental state change, hallucination, vision and speech problem, seizure, stroke, and balance disturbance.

Nalleballe, et al. have described the spectrum of neuropsychiatric manifestations associated with COVID-19 in a study of a total of 40,469 COVID-19 patients that reported 9,086 (22.5%) patients who had neuropsychiatric manifestations [13]. Their study reported the following:

- Headaches were the most common neurologic manifestations that were reported in 1501 (3.7%), followed by sleep disorders reported in 1394 (3.4%) patients.
- Other manifestations were encephalopathy 937 (2.3%); myalgia 821 (2.0%); pain 723 (1.8%); loss of taste and smell 477 (1.2%); stroke and transient ischemic attack 406 (1.0%); dizziness 379 (0.9%); extrapyramidal and movement disorders 277 (0.7%); seizures 258 (0.6%); polyneuropathy 247 (0.6%); and nerve root and plexus disorders 145 (0.4%).

Another study of six-months neurological and psychiatric outcomes in survivors of COVID-19 provided estimates of the risks of neuropsychiatric disorders in the six months after a COVID-19 diagnosis, using the EHRs of over 236,000 patients with COVID-19. It reported the incidence and hazard ratios of these conditions compared with patients who had had

influenza or other respiratory tract infections. It also showed that both incidence and hazard ratios were greater in patients who required hospitalization or admission to the intensive care unit and in those who had encephalopathy (delirium and other altered mental states) during the illness compared with those who did not [4], [14]–[16]. The incidence of psychiatric or neurological diagnosis, six months post-infection, was found to be 33.62%, with 12.84% being diagnosed for the first time. For patients admitted to ICU, 46.42% were diagnosed with neurological or psychiatric disorders six months after the disease. Among these individuals,

25.79% (23.50–28.25) had no history of these diseases. This research also showed a significantly increased risk of psychotic disorders. Substance use disorders and insomnia were more common in those with COVID-19 than those who suffered from influenza or other respiratory tract infections. The research also showed that compared to neurological disorders, mood and anxiety disorders showed a weaker relationship with the markers of COVID-19 severity in terms of incidence or hazard ratios. This may be because their occurrence is due to a psychological implication of the COVID-19 diagnosis rather than a direct manifestation of the disease.

Potential mechanisms of neuropsychiatric manifestations in COVID-19 include [17]:

- Viral infiltration into the central nervous system.
- Cytokine network dysregulation,
- Peripheral immune cell transmigration.
- Post-infectious autoimmunity.

Beach, et al. have described two hypotheses of encephalopathy pathogenesis in COVID-19 [18]. The first hypothesis they describe is the primary neuro-invasive hypothesis. Two mechanisms for causing primary encephalopathy exist within this hypothesis. The first is the virus invading the brain via a synapse-connected pathway extending from chemo and mechanoreceptors in the lung to the medullary cardiorespiratory center. The second is the virus invading the olfactory bulb. This mechanism could explain the rates of anosmia and ageusia. The second hypothesis described is the secondary systemic mechanism. Two mechanisms described within this hypothesis include acute respiratory distress syndrome (ARDS) mediated and immune response mediated. In ARDS hypoxemia, oxidative stress from ARDS, hypoperfusion, and uremia from multi-organ failure in the setting of ARDS, and cardiovascular accidents could lead to encephalopathy. The second mechanism, the immune response mediated, could occur via cytokine storm with BBB breakdown or endothelial transfer. The final hypothesis is the hybrid model. In this model, the virus may cause either a primary or secondary encephalopathy or both. In this model Beach et al. compare the similarities between HIV and COVID. They suggest that if the SARS-CoV-2 virus enters the brain by disrupting the circumventricular fenestrated endothelium or up an olfactory nerve track then it might have a similar pathophysiological pathway to HIV encephalopathy.

In a study focusing on nervous system involvement and infection with COVID-19 and other coronaviruses, Wu et al. provided different pathways by which coronaviruses could invade the blood-brain barrier (BBB) and lead to neuropsychiatric sequela [19]. The pathogenesis of CNS injury includes infectious toxic encephalopathy, viral encephalitis, and acute cerebrovascular disease. Infectious toxic encephalopathy, also referred to as acute toxic encephalitis, involves a reversible brain dysregulation caused by systemic toxemia,

metabolic abnormalities, and hypoxia in the setting of acute infection [20]–[22]. The pathological changes of the disease involve cerebral edema while the clinical symptoms vary from headache and dysphoria to delirium. Some patients have more serious symptoms and present with disorientation, loss of consciousness, coma and paralysis [20], [23]. Acute viral infection is associated with respiratory symptoms and hypoxia that could lead to toxic encephalopathy [24].

Viral encephalitis causes inflammatory changes to brain tissue by direct viral pathogen damage to neurons and surrounding tissue. Symptoms commonly seen involve headaches, fever, vomiting, convulsions and changes in consciousness [25]. Xiang et al. were able to detect SARS-CoV-2 in the CSF of patients with COVID-19 by genome sequencing, therefore, confirming that COVID-19 can affect the central nervous system leading to encephalitis [8].

Acute cerebrovascular disease can also be a consequence of COVID-19. Severely ill patients with SARS-CoV-2 often have high D dimer levels and low platelets making these patients more susceptible to acute cerebrovascular events [26]. SARS CoV-2 has been widely known to cause cytokine storm which could also be a precipitating factor leading to cerebrovascular disease [27], [28].

Viruses can infect macrophages, microglia and astrocytes in the CNS. Neurotropic viruses can activate glial cells leading to a pro-inflammatory state [29]. Wan et al. observed that interleukin 6 (IL-6) was positively correlated with the severity of COVID-19 symptoms [30]. Bohmwald et al., has demonstrated that glial cells in vitro can secrete large amounts of inflammatory markers such as IL-6, IL-12, IL-15, and TNF- α after being infected with CoV [31].

Angiotensin-converting enzyme 2 (ACE-2) is an enzyme found in several organs such as the lungs, heart and CNS and plays a significant role in blood pressure regulation [32]. ACE-2 is also an enzyme targeted by CoV and influenza viruses [33]–[35]. Binding to ACE2 can lead to elevated blood pressure and as a consequence cerebral vascular accidents. Since ACE2 is also expressed in capillary endothelium the virus can bind to ACE2 leading to damage of the blood-brain barrier and entrance into the CNS [36].

Toll-like receptors (TLRs) also play a role in the pathogenesis of COVID-19 [37]. The Toll-like receptor family has ten identified members in humans TLR1-TLR10 [38]. These ten receptors play a vital role in the activation of innate immunity, cytokine regulation and identification of pathogen-associated molecular patterns on bacteria, viruses and other parasites [38]–[41]. Toll-like receptors are located on several immune cells, namely dendritic cells, macrophages and natural killer cells [37]. COVID-19 is a single-stranded RNA virus with four key proteins. These four proteins are a spike (S) protein, an envelope (E) protein, membrane (M) and nucleocapsid (N) [38]. SARS-CoV-2 Spike protein is the protein that binds on the ACE2 receptor [37], [38]. Toll-like receptor 7/8 identifies single-stranded RNA viruses such as COVID-19 [37], [38]. Activation of TLR 7/8 is then followed by the release of IL-1, IL-6, TNF- α , monocyte chemoattractant protein – 1 (MCP-1), macrophage-inflammatory protein 1 alpha (MIP-1 A) and interferon-gamma IFN-gamma [42]. Cytokine storm causing an amplified cytokine production can lead to acute respiratory distress syndrome (ARDS) [43] and multiple organ dysfunction syndrome (MODS) which can also explain CNS involvement secondary to an inflammatory response [26]. Therefore, future therapeutic modalities (medications or vaccines) could focus on targeting TLR-7/8 [37], [38], [44]. Given the above pathways, the concern is that CoV can lead to persistent

neuropsychiatric diseases and systemic inflammation warranting continued monitoring and management.

The Role of Stress in Facilitating Psychiatric Disorders:

Public health emergencies can affect the health, safety, and well-being of both individuals (e.g., insecurity, confusion, emotional isolation, and stigma) and communities (owing to economic loss, work and school closures, inadequate resources for medical response, and deficient distribution of necessities). A stress response is triggered when a stressor is perceived as a threat or challenge. Stress during a pandemic can cause fear and worry about our health and the health of our loved ones, our financial situation or job, or the loss of support services we rely on. Everyone reacts differently to stressful situations. Stress can be adaptive (“normal”), manageable, or maladaptive. It can also cause changes in sleep or eating patterns, difficulty sleeping or concentrating, worsening of chronic health problems worsening of mental health conditions, increased use of tobacco, alcohol, and other substances. Extensive research in disaster mental health has established that emotional distress is common in affected populations, a finding that is already being echoed in populations affected by the COVID-19 pandemic.

This stress-mediated pathway is best explained by the stress diathesis model where a disorder develops from a genetic predisposition for that illness combined with stressful conditions that play a precipitating or facilitating role [45].

The stress response begins in the brain where the amygdala sends a distress signal to the hypothalamus which in turn functions like the command center communicating with the rest of the body through the nervous system triggering a fight, flight, or fear response. This response, especially the extreme fear and uncertainty are two that have become more evident in society. Both of these responses contribute to a heightened stress response that is likely to manifest as follows [6]:

1. Stress is likely to precipitate an acute exacerbation of an existing disorder.
2. Precipitate a first-time episode of a disorder in those who are predisposed to it due to a biological or genetic vulnerability (stress-diathesis model).
3. Trauma or stressor-related disorder (e.g., acute stress disorder, posttraumatic stress disorder, or an adjustment disorder).
4. Symptomatic stress response that does not meet the diagnostic criteria of a formal psychiatric disorder.

Social isolation, anxiety, fear of contagion, uncertainty, chronic stress and economic difficulties may lead to the development or exacerbation of stress-related disorders and suicidality in vulnerable populations. The increase in the prevalence of psychiatric conditions and symptoms is not new as suggested by previous outbreaks. In the Spanish Flu pandemic caused by the H1N1 virus in 1918–1919, there was an associated increase in death by suicide [46]. In the Hong Kong SARS outbreak in 2003, there was a significant increase in suicide death amongst people ages 65 and older [47]. Patients with preexisting psychiatric disorders are likely to have increased symptoms and should be monitored for breakthrough symptoms and acute exacerbations. Studies have shown an association between the elevated

incidence of suicidal behavior and the development of psychiatric disorders in individuals with low resilience [48]–[52]. Sher L recommends mental health professionals should educate the general public regarding issues related to resilience and stress-coping. Promoting resilience in the general population may reduce suicide rates. Suicide risk among psychiatric patients may be reduced by improving resilience and therefore, should be part of every psychiatric patient's treatment plan.

Regarding suicidality, there was an encouraging JAMA report, based on data from the CDC's National Center for Health Statistics that showed that a total of 44,834 deaths by suicide occurred in 2020, a decrease of 5.6% from the 47,511 suicides in 2019 [53]. The overall number of deaths increased by 503,976 (17.7%) in 2020, with 345,323 of those attributable to COVID-19. While the reported decrease in deaths by suicide is encouraging, we need to remain cautious since much remains unknown about the impact of COVID-19 on suicides.

Also, suicide is complex, and an individual's risk factors combined with precipitants such as evolving experiences with isolation, depression, anxiety, economic stress, and suicidal ideation and access to lethal means may lead to periods of increased risk. It has also been observed that suicide rates tend to decline in the wake of a collective, community trauma. The reason is unknown, but some hypotheses include the possibility that individuals become more externally focused given the environmental threat, that the community cohesion that sometimes follows catastrophe has beneficent effects, or that community suffering makes personal suffering more tolerable.

Post-COVID-19 Neuropsychiatric Sequelae

Patients who recover from acute COVID-19 can experience a variety of neuropsychiatric manifestations [54], [55]. For individuals with mild to moderate infections, the most common symptoms include headache, altered smell and taste, cough, asthenia, and myalgia. When severe illness occurs, reports of encephalopathies, encephalitis, seizures, neuromuscular disorders, Guillain-Barre´ syndrome, and other neuropathies were reported in about 36% of patients [54], [55].

Chronic neuropsychiatric manifestations have been described with other viral infections, e.g., HSV-1,2,6,8; VZV: enteroviruses, EBV; and adenovirus. Encephalopathy associated with HIV has been well documented. There have also been reports of encephalitis lethargica and post-encephalitic Parkinsonism. "Mental fog" and fatigue associated with severe sub-acute encephalopathy requiring lengthy rehab in patients after long ventilator treatment for COVID-19 ARDS has been reported. If this can result in chronic encephalopathy (dementia) is still not determined. In the current COVID-19 pandemic, clinicians should be alert to the possibility of long-term chronic neurodegenerative states we call dementias.

Given that a large number of patients with COVID-19 experience severe respiratory distress requiring intensive care unit (ICU) treatment, we should also be cognizant of the literature that already exists on the "Post-Intensive Care Syndrome." In a study of patients who were admitted to the (ICU), researchers found a number of long-term effects [56], including:

- Patients in the ICU with ARDS and severe illness (91% on ventilation) had average global cognition scores 1.5 standard deviations (SD) below the age-adjusted mean

population and were similar to patients with mild cognitive impairment. Of those patients, 26% had 2 SD below the normal.

- Patients with mild Alzheimer disease and repeated testing at 12 months later did not show significant improvement.
- Cognitive impairment was noted in 70–100% of discharged patients, 46–80% had impairment 1 year and even 5 years later, and 20% had residual cognitive dysfunction.

If patients admitted to the ICU with COVID-19 follow these trends, they will feel the virus' effects for years to come.

COVID 19 and mental health long Haulers

In 2019 between April and June 11% of Americans reported anxiety and or depression according to the national center for health statistics national health interview survey [57]. During the same time interval in 2020 when Covid 19 was affecting the US population 35.6% of Americans reported symptoms of anxiety and depression according to the centers for disease control and prevention household pulse survey [58].

Long haulers are people experiencing long-term symptoms of COVID-19. The symptoms include both physical and mental health symptoms [59]. Some of the other names describing this condition include long COVID-19 long-haul covid 19 and post-acute COVID-19. The National Institute of Health has described this as a post-acute sequela of SARS-CoV-2 infection (PASC) [60].

A recent study published in the Lancet psychiatry determined that one in three patients who recovered from COVID-19 later presented with neurologic or psychiatric conditions within six months of the infection with anxiety and depression being the most common on that list [4]. An article published in the Journal of Affective disorders demonstrated that people with higher mental resilience developed less mental distress during the pandemic compared to people with lower resilience [61].

Psychiatric vulnerability is also a contributing factor when determining who will develop long-term mental health complications and who will be resilient. Dudley et al., studied vulnerability and resilience to psychiatric disorders. In his study epigenetic changes such as DNA methylation, acetylation and histone changes contributed to changes in DNA gene expression leading to psychiatric vulnerability [62].

It has almost been two years since the pandemic started and the extent of the COVID-19 impact has not yet been fully appreciated although it will likely be consequential with 208 million cases and 4.38 millions of deaths [63], [64].

The effects of COVID-19 are expected to at times persist longer than 4 weeks from the onset of infection. COVID-19 is recognized as a multiorgan viral infection with several manifestations [65]. According to Nalbandian et al., PASC is considered as a multiorgan condition that likely involves poorly regulated immune response, inflammation, microvascular thrombosis and cell damage [66]. PASC involves a group of symptoms that range in severity [67]. Some of these symptoms are dyspnea, cough, racing heartbeat, fatigue, weakness, pain, dizziness, difficulty thinking and memory problems, sleep disturbance, depression, anxiety, PTSD [67].

Of the patients hospitalized with COVID-19 approximately $\frac{3}{4}$ had at least one persistent symptom 6 months after the acute infection, [68] and 30% had persistent symptoms at 9 months [69]. Long-term symptoms included persistent neurological and psychiatric concerns [70]. The medical community is now faced with the challenge of how to best take care of these patients in the future. This challenge will also give rise to the opportunity to integrate a medical and psychiatric approach to the care of patients with PASC.

Several studies indicated the long-term implications of COVID and the need for continued monitoring of this patient population. Given that the pandemic is still ongoing and more people are contracting covid that will require long-term care, attention and consideration has to be given to the physicians that will be tasked with treating patients with PASC.

Discussion

In this review we have described, with supporting evidence, how COVID-19 can impact the brain and mind, both acutely and long term. While the long-term effects have not yet been clearly defined or determined, studies have shown that people afflicted by this virus will likely continue to experience neuropsychiatric symptoms for months to years to come.

Given the evidence we have summarized regarding the neuropathologic processes associated with COVID in this paper, there are several areas that the mental health clinician may need to keep in mind in the course of their examination of patients with COVID-related symptoms.

1. It is important that the healthcare providers are aware that COVID-19 patients often experience neuropsychiatric symptoms, especially in more severe cases. It is also important that clinical providers have an effective clinical approach to working up a patient experiencing these neuropsychiatric symptoms.
2. When patients are suspected or confirmed to have COVID-19, it is important to evaluate for potential neuropathologic processes that have been seen with this virus, including delirium, cerebrovascular events, encephalitis or encephalopathy, mental status changes and new neurologic symptoms.
3. Developing a multidisciplinary team approach to manage the psychiatric and behavioral disturbances that may arise from neuropsychiatric manifestations of COVID-19. This includes liaising with relevant medical professionals, as well as acting as a part of the multidisciplinary team to manage exacerbation of psychiatric and behavioral disturbances arising from neuropsychiatric complications.
4. Developing an effective clinical approach to managing acute behavioral disturbance using bio-psychosocial strategies. This includes judicious use of medications as patients with organic brain illness may be more susceptible to side effects. Diagnosis of new onset psychiatric disorders and adjustments of treatment, when needed, are both part of developing this clinical approach.
5. Identification and management of relapses or exacerbation of illness due to the pandemic in a vulnerable population. Making sure stress does not precipitate new episodes in those who are currently stable on maintenance treatment.
6. In the aftermath of pandemics, increased psychiatric screening and surveillance is recommended to address psychiatric presentations, including neuropsychiatric syndromes.

We encourage physicians to focus on both medical and neuropsychiatric aspects of the disease, while realizing that often the two are intertwined. Studies have also shown that people afflicted by this virus will likely continue to experience neuropsychiatric symptoms for months to years to come, which will require the healthcare providers continue monitoring for such symptoms.

It remains to be seen how the neuropsychiatric symptom burden will ultimately impact our service delivery, both at the patient and population levels. However, it would make sense to be proactive and plan for services that are equipped to identify and effectively manage cases of Long COVID.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11126-022-09980-9>.

Ethical Approval This article does not contain any studies with human participants or animals performed by any of the authors.

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